Early Prevention of Atherosclerosis

ARTERIOSCLEROTIC CARDIOVASCULAR DISEASE remains the leading cause of death in the United States and in most of the other industrialized nations of the world. Extensive prospective epidemiologic studies have identified a number of characteristics of the coronary-prone subject. Among those factors associated with the greatest increments of risk are hyperlipidemia, hypertension and smoking, all of which potentially may be modified. In fact, the residual risk associated with a family history of coronary disease is small when the risk increments attributable to these factors are removed. These findings have stimulated a number of intervention studies, using dietary modification or drugs, in which the majority of subjects, however, have been in or beyond the fifth decade of life. Nevertheless, moderate decreases in the incidence of new coronary events or of death from coronary heart disease have accompanied dietary modifications which result in significant reduction of serum cholesterol levels.[1,2] The results of drug treatment of patients with previous myocardial infarctions have varied from moderate decreases in mortality for certain patient subgroups[3,4] to little discernible effect.[5] The finding that atherosclerotic changes are often present in the coronary arteries even in patients in their early twenties[6,7] indicates that measures directed at primary prevention in the general population will have to be begun during adolescence, and probably earlier for persons with primary hyperlipoproteinemias. The statement of position by the California Society of Pediatric Cardiology and the California Heart Association which appears in this issue of the JOURNAL endorses this view.

Recent progress in the investigation of mechanisms of atherogenesis lends support to the belief that the three principal risk factors enumerated above reflect important elements in the process of plaque formation. That blood platelets interact with injured arterial endothelium, resulting in hyperplasia of smooth muscle elements in the arterial wall, is now appreciated.[8] Modification of platelet behavior by hyperlipidemia[9] may amplify this platelet-dependent process as well as thrombogenesis. Accumulation of lipids from lipoproteins containing apolipoprotein B, which has a demonstrable affinity for certain connective tissue elements,[10] appears to account for the initial appearance of lipid in the lesion. Thus, elevated levels of either beta (low density) or prebeta (very low density) lipoproteins in serum would be expected to accelerate this process. Hypertension leads to vascular injury. Smoking exerts effects on plasma free fatty acids and upon platelet behavior in addition to its hemodynamic effects. The association of elevated levels of beta and prebeta lipoproteins (but not of high density lipoproteins), with accelerated appearance of coronary vascular disease is amply confirmed by available epidemiologic data.

The question of whether early prospective modification of these factors will significantly reduce the ultimate risk of coronary vascular disease cannot yet be given a definitive answer for our population. However, the intimate relationship of risk factors identified in epidemiologic studies with essential elements in the process of atherogenesis, along with the remarkably lower incidence of coronary disease in populations in which plasma lipid levels are much lower, suggests that such modification is likely to be efficacious. Clearly, treatment of hypertension and abstention from smoking result in demonstrably reduced morbidity and mortality. Attempts to modify serum lipoprotein levels by changes in diet, even in childhood, appear indicated as well, since surveys of children and adolescents in the United States show serum cholesterol levels much higher than those found in age-matched populations in countries with lower incidences of coronary disease.[11,12]

Beyond caloric restriction, the simplest dietary modification is restriction of the daily intake of cholesterol to approximately 300 mg. This would be expected to result in a reduction of 10 to 15 percent in serum cholesterol levels. A further decrement of similar magnitude can be obtained by sharp restriction of saturated fat, an objective much harder to achieve because of prevailing American dietary habits. However, profound modification of diet probably should not be undertaken in infancy—or even in the first four or five years of life—until more is understood about the nutrition of the very young.

While the measures outlined above are prob-

ably sufficient for the general population, primary hyperlipidemia presents a special situation even in childhood. Since the primary forms of hypertriglyceridemia generally tend to appear in the early adult years, the predominant form of genetic hyperlipidemia in childhood is hyperbetalipoproteinemia. Many persons with this pattern of hyperlipoproteinemia are now known to carry one or more dominant genes for defective binding of beta lipoprotein to cell membranes.[13] Persons with elevated levels of beta lipoprotein can be identified by measurement of serum cholesterol level alone, obviating the requirement for fasting. Since most persons with this disorder are asymptomatic in childhood and since its prevalence probably exceeds one-tenth percent in our population, measurement of serum cholesterol levels is reasonable in multiphasic screening of children. Clearly, all children should be studied in kindreds in which early coronary vascular disease, hyperlipidemia or xanthomatosis occur.

The response of many persons with primary hyperbetalipoproteinemia to modifications in diet is disappointing. Since this disorder results in demonstrable acceleration of coronary atherogenesis,[14] combined diet and drug treatment in childhood may be indicated. Drug treatment of children heterozygous for hyperbetalipoproteinemia should still be regarded as experimental, with emphasis on the identification of effective agents. However, the fulminant atherogenesis encountered in homozygotes requires energetic treatment with the most effective regimen now available. This appears to be a combination of bile acid-binding resin and nicotinic acid.[15]

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PSRO Update—1975

IT IS NOW more than two years since PL 92-603 with its mandate for Professional Standards Review Organizations (PSROs) became the law of the land. The two hundred and three PSRO areas were established on schedule. Much of the overt opposition has subsided but quite considerable disquiet and uncertainty remain. And they will remain until there is some indication of whether the overall effect of PSRO implementation will improve patient care or impair it—and if it does improve it, whether the cost in time and dollars to operate the inevitably cumbersome machinery will prove to be worth the benefit. It is safe to say that many practicing physicians remain skeptical and unconvinced.

The establishment of local PSROs is in progress but it is proceeding more slowly than called for by the law. It appears that by January 1, 1976 (the date when the Secretary of Health, Education, and Welfare becomes empowered to establish PSROs in areas which do not yet have them), only about one half or two thirds of the designated areas will have local PSRO organizations which will qualify for conditional or planning status under the law. This slowness is at least in part due to inadequate federal funding for the program.

There are a number of other problems in the planning for PSROs which so far have not been re-